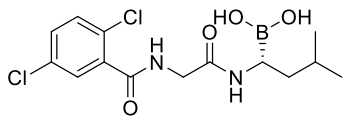
Product data sheet

MedKoo Cat#: 205857 Name: Ixazomib (MLN-2238) CAS#: 1072833-77-2 (free) Chemical Formula: $C_{14}H_{19}BCl_2N_2O_4$ Exact Mass: 360.08149 Molecular Weight: 361.02866	
Product supplied as:	Powder
Purity (by HPLC):	≥ 98%
Shipping conditions	Ambient temperature
Storage conditions:	Powder: -20°C 3 years; 4°C 2 years.
	In solvent: -80°C 3 months; -20°C 2 weeks.

1. Product description:
Ixazomib, also known as MLN-2238, is a potent proteasome inhibitor (PI) with potential antineoplastic activity. MNL-2238 is also .the biologically active form of MLN9708. MLN2238 has an improved pharmacodynamic profile and antitumor activity compared with bortezomib in both OCI-Ly10 and PHTX22L models. Although both MLN2238 and bortezomib prolonged overall survival, reduced splenomegaly, and attenuated IgG2a levels in the iMyc(Cα)/Bcl-X(L) GEM model, only MLN2238 alleviated osteolytic bone disease in the DP54-Luc model.

2. CoA, QC data, SDS, and handling instruction
SDS and handling instruction, CoA with copies of QC data (NMR, HPLC and MS analytical spectra) can be downloaded from the product web page under "QC And Documents" section. Note: copies of analytical spectra may not be available if the product is being supplied by MedKoo partners. Whether the product was made by MedKoo or provided by its partners, the quality is 100% guaranteed.

3. Solubility data

Solvent	Max Conc. mg/mL	Max Conc. mM
DMSO	67.25	186.27
Ethanol	72.0	199.43

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.77 mL	13.85 mL	27.70 mL
5 mM	0.55 mL	2.77 mL	5.54 mL
10 mM	0.28 mL	1.38 mL	2.77 mL
50 mM	0.06 mL	0.28 mL	0.55 mL

5. Molarity Calculator, Reconstitution Calculator, Dilution Calculator
Please refer the product web page under section of "Calculator"

6. Recommended literature which reported protocols for in vitro and in vivo study
In vitro study

1. Roeten MSF, van Meerloo J, Kwidama ZJ, Ter Huizen G, Segerink WH, Zweegman S, Kaspers GJL, Jansen G, Cloos J. Pre-Clinical Evaluation of the Proteasome Inhibitor Ixazomib against Bortezomib-Resistant Leukemia Cells and Primary Acute Leukemia Cells. Cells. 2021 Mar 17;10(3):665. doi: 10.3390/cells10030665. PMID: 33802801; PMCID: PMC8002577.
2. Wang Q, Dong Z, Su J, Huang J, Xiao P, Tian L, Chen Y, Ma L, Chen X. Ixazomib inhibits myeloma cell proliferation by targeting UBE2K. Biochem Biophys Res Commun. 2021 Apr 16;549:1-7. doi: 10.1016/j.bbrc.2021.02.048. Epub 2021 Feb 26. PMID: 33647537.

In vivo study

1. Sánchez G, Chalmers S, Ahumada X, Montecinos L, Olmedo I, Eisner V, Riveros A, Kogan MJ, Lavandero S, Pedrozo Z, Donoso P. Inhibition of chymotrypsin-like activity of the proteasome by ixazomib prevents mitochondrial dysfunction during myocardial ischemia. PLoS One. 2020 May 26;15(5):e0233591. doi: 10.1371/journal.pone.0233591. PMID: 32453773; PMCID: PMC7250417.

2. Harris MA, Miles MA, Shekhar TM, Cerra C, Georgy SR, Ryan SD, Cannon CM, Hawkins CJ. The Proteasome Inhibitor Ixazomib Inhibits the Formation and Growth of Pulmonary and Abdominal Osteosarcoma Metastases in Mice. Cancers (Basel). 2020 May 11;12(5):1207. doi: 10.3390/cancers12051207. PMID: 32403415; PMCID: PMC7281181.

7. Bioactivity

Biological target:

Ixazomib (MLN2238) inhibits the chymotrypsin-like proteolytic (β5) site of the 20S proteasome with an IC50 of 3.4 nM (Ki of 0.93 nM).

In vitro activity

To further examine the molecular mechanism through which ixazomib blocks cell proliferation, the effects of the drug on mitosis- and apoptosis-related genes was investigated. As shown in Fig. 4, ixazomib decreased the protein levels of cyclin E1, cyclin D1, and Bcl-2 in RPMI-8226 and U-266 cells. The reduction of cyclin E1, cyclin D1 and Bcl-2 protein levels by ixazomib was relieved by UBE2K transfection. Alternatively, ixazomib increased the protein levels of cyclin B1, McL-1, and PARP1 in cells, while UBE2K transfection blocked ixazomib's effects. These findings demonstrate that ixazomib regulates mitosis- and apoptosis-related genes by lowering UBE2K expression, which leads to reduce proliferation of myeloma cells.

Reference: Biochem Biophys Res Commun. 2021 Apr 16;549:1-7.
https://www.sciencedirect.com/science/article/pii/S0006291X21002321?via%3Dihub

In vivo activity

Unlike the KRIB metastatic model, only ixazomib reduced the growth of 143B lung tumors whereas bortezomib was ineffective (Figure 5A). Ixazomib, not bortezomib, also delayed the formation of abdominal metastases (liver and/or kidneys) compared to saline (Figure 5B). Ixazomib-treated mice survived longer and some were asymptomatic at the endpoint of the experiment, whereas most saline- and bortezomib-treated mice required euthanasia due to intolerable tumor-related symptoms (Figure 5C–E). The most striking difference between ixazomib, compared to saline and bortezomib, was the reduced overall tumor burden in the lungs, liver and kidneys ex vivo (Figure 5E). The ex vivo bioluminescence of the lungs in ixazomib-treated mice was at least 100-fold lower than the mice treated with saline or bortezomib, despite being culled up to 21 days later.

Reference: Cancers (Basel). 2020 May; 12(5): 1207. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7281181/

Note: The information listed here was extracted from literature. MedKoo has not independently retested and confirmed the accuracy of these methods. Customer should use it just for a reference only.